Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	774	544/58.2, 514/227.8	USPAT	OR	OFF	2005/08/30 16:05
L2	426	544/58.2, 514/227.8	US-PGPUB	OR	OFF	2005/08/30 16:05
L4	1200	544/58.2, 514/227.8	US-PGPUB; USPAT	OR	OFF	2005/08/30 16:05

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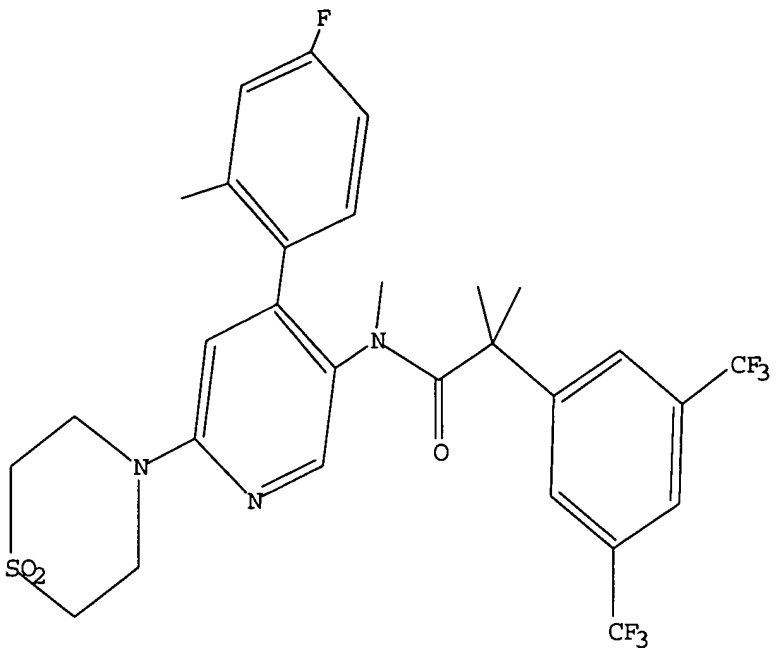

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

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SEARCH TIME: 00.00.01

L3            2 SEA SSS FUL L1

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COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
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FULL ESTIMATED COST 161.33 161.54

FILE 'CAPLUS' ENTERED AT 12:45:50 ON 30 AUG 2005
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FILE COVERS 1907 - 30 Aug 2005 VOL 143 ISS 10
FILE LAST UPDATED: 29 Aug 2005 (20050829/ED)

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L4 5 L3

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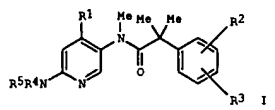
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:29200 CAPLUS
DOCUMENT NUMBER: 142:134463
TITLE: Preparation of 2-phenyl-N-(pyridin-3-yl)-N-methylisobutyramide derivatives as dual NK1/NK3 antagonists for treating schizophrenia
INVENTOR(S): Hoffmann, Torsten; Koblet, Andreas; Peters, Jens-Uwe; Schnider, Patrick; Sleight, Andrew; Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005002577	A1	20050113	WO 2004-EP6929	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005090533	A1	20050428	US 2004-884707	20040702
PRIORITY APPLN. INFO.:			EP 2003-14513	A 20030703
OTHER SOURCE(S):		MARPAT 142:134463		

GI

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



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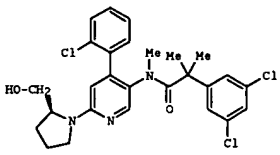


II

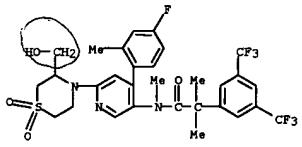
AB The invention is directed to the use of compds. of formula I [wherein R1 = (un)substituted aryl; R2, R3 = independently H, halo, alkyl, alkoxy, OCHF2, OCH2F, OCF3, or CF3; R4, R5 = independenlty H, CHO, (CH2)oS(O)p-alkyl, etc.; o = 0-3; p = 0-2; or R4NR5 form an (un)substituted ring with -(CH2)3-5-, -(CH2)1,2,3-O-(CH2)2-, -CH2CH:CHCH2-, etc.;] and their pharmaceutically active acid addition salts as dual neurokinin NK1/NK3 antagonists useful in the treatment of schizophrenia. The invention discloses 421 prepns. of title compds. For example, II was prepared, in 2 steps, by acylation of N-[6-chloro-4-(2-chlorophenyl)pyridin-3-yl]methylamine (preparation given) with 2-(3,5-dichlorophenyl)-2-methylpropanoyl chloride (preparation given) and amination with (L)-prolinol. II bound to NK1 and NK3 receptors with pKi value of 8.47 and 9.05, resp.

IT **825641-09-6P**, 2-[3,5-Bis(trifluoromethyl)phenyl]-N-[4-(4-fluoro-2-methylphenyl)-6-(3-hydroxymethyl-1,1-dioxo-4-thiomorpholinyl)pyridin-3-yl]-N-methylisobutyramide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-(pyridin-3-yl)-N-methylisobutyramide derivs. as dual NK1/NK3 antagonists for treating schizophrenia)

RN 825641-09-6 CAPLUS
CN Benzeneacetamide, N-[4-(4-fluoro-2-methylphenyl)-6-[3-(hydroxymethyl)-1,1-dioxido-4-thiomorpholinyl]-3-pyridinyl]-N,α,α-trimethyl-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)

own work

L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:648391 CAPLUS
DOCUMENT NUMBER: 141:174195
TITLE: A preparation of new crystalline modifications of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide, useful as NK1 receptor antagonists
INVENTOR(S): Hoffmann, Torsten; Hoffmann-Emery, Fabienne; Nick, Sonia; Schwitter, Urs; Waldmeier, Pius
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067007	A1	20040812	WO 2004-EP547	20040123
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
US 2004186100	A1	20040923	US 2004-766122	20040127
PRIORITY APPLN. INFO.:			EP 2003-2134	A 20030131

GI

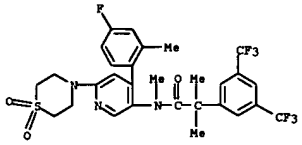
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of new crystalline modifications of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methyl-isobutyramide (I) characterized by X-ray diffraction and useful as NK1 receptor antagonists. I was prepared via amidation of the obtained propionic acid derivative II by thiomorpholinylpyridine derivative III and subsequent S-oxidation Four modifications of I were identified: 3 crystalline (A, B, C) and one amorphous. Form A demonstrated the highest bioavailability among the three crystalline polymorphs A, B, and C.

IT **474026-04-5P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new crystalline modifications of thiomorpholinylpyridine derivative, useful as NK1 receptor antagonists)

RN 474026-04-5 CAPLUS
CN Benzeneacetamide, N-[6-(1,1-dioxido-4-thiomorpholinyl)-4-(4-fluoro-2-methylphenyl)-3-pyridinyl]-N,α,α-trimethyl-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:610660 CAPLUS
DOCUMENT NUMBER: 139:160766
TITLE: A method for correlating the preprotachykinin gene (NKNA) polymorphisms with the efficacy and compatibility of a pharmaceutically active compounds, such as NK-1 receptor antagonists
INVENTOR(S): Foernzler, Dorothee; Hashimoto, Lara; Li, Jia; Luedin, Eric; Sleight, Andrew; Vankan, Pierre
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003064685	A2	20030807	WO 2003-EP630	20030123
WO 2003064685	A3	20031224		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2473128	AA	20030807	CA 2003-2473128	20030123
EP 1472377	A2	20041103	EP 2003-734685	20030123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007257	A	20041214	BR 2003-7257	20030123
JP 2005515788	T2	20050602	JP 2003-564275	20030123
US 2003158187	A1	20030821	US 2003-354693	20030130

PRIORITY APPLN. INFO.: EP 2002-1937 A 20020131
WO 2003-EP630 W 20030123

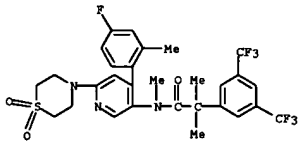
AB The present invention relates to a method for correlating single nucleotide polymorphisms in the preprotachykinin (NKNA) gene with the efficacy and compatibility of a pharmaceutically active compound administered to a human being. The invention further relates to a method for determining the efficacy and compatibility of a pharmaceutically active compound administered to a human being which method comprises determining at least one single nucleotide polymorphism in the NKNA gene. Said methods are based on determining specific single nucleotide polymorphisms in the NKNA gene and determining the efficacy and compatibility of a pharmaceutically active compound in the human by reference to polymorphism in NKNA. The invention further relates to isolated nucleic acids comprising within their sequence the polymorphisms as defined herein, to nucleic acid primers and oligonucleotide probes capable of hybridizing to such nucleic acids and to a diagnostic kit comprising one or more of such primers and probes for

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

detecting a polymorphism in the NKNA gene, to a pharmaceutical pack comprising neurokinin-1 (NK-1) receptor antagonists and instructions for administration of the drug to human beings tested for the polymorphisms as well as to a computer readable medium with the stored sequence information for the polymorphisms in the NKNA gene.

IT **474026-04-5**
RL: ANT (Analyte); PAC (Pharmacological activity); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NK-1 receptor antagonist; method for correlating preprotachykinin gene (NKNA) polymorphisms with efficacy and compatibility of pharmaceutically active compds., such as NK-1 receptor antagonists)

RN 474026-04-5 CAPLUS
CN Benzeneacetamide, N-[6-(1,1-dioxido-4-thiomorpholinyl)-4-(4-fluoro-2-methylphenyl)-3-pyridinyl]-N,α,α-trimethyl-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:117823 CAPLUS
DOCUMENT NUMBER: 138:170243
TITLE: Preparation of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(2-methyl or 4-fluoro-2-methyl substituted)phenyl-pyridin-3-yl]-N-methyl-isobutyramide as selective NK1 antagonists
INVENTOR(S): Ballard, Theresa Maria; Hoffmann, Torsten; Poli, Sonia Maria; Schnider, Patrick; Sleight, Andrew
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011860	A2	20030213	WO 2002-EP8311	20020726
WO 2003011860	A3	20030904		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003064983	A1	20030403	US 2002-196795	20020717
US 6849624	B2	20050201		
CA 2452502	AA	20030213	CA 2002-2452502	20020726
EP 1414525	A2	20040506	EP 2002-791471	20020726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011523	A	20040914	BR 2002-11523	20020726
CN 1537025	A	20041013	CN 2002-815110	20020726
JP 2005500354	T2	20050106	JP 2003-517052	20020726

PRIORITY APPLN. INFO.: EP 2001-118412 A 20010731
WO 2002-EP8311 W 20020726

OTHER SOURCE(S): MARPAT 138:170243
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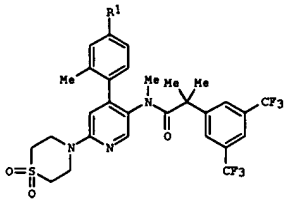
L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



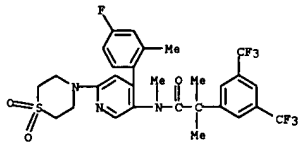
I

AB The title compds. I [R1 = H, F] which may be used for the treatment of migraine, rheumatoid arthritis, asthma, bronchial hyperreactivity, inflammatory bowel disease or for the treatment of disorders including Parkinson's disease, anxiety, depression, pain, headache, Alzheimer's disease, multiple sclerosis,edema, allergic rhinitis, Crohn's disease, ocular injury, ocular inflammatory diseases, psychosis, motion sickness, induced vomiting, emesis, urinary incontinence, psychoimmunol. or psychosomatic disorders, cancer, withdrawal symptoms of addictive drugs from opiates or nicotine, traumatic brain injury or benign prostatic hyperplasia, were prepared and formulated. E.g., a 8-step synthesis of I [R1 = H] (starting with 2-chloro-5-nitropyridine and thiomorpholine) which showed pKi of 8.9 for the human NK1 receptor, was given.

IT **474026-04-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(2-Me or 4-fluoro-2-Me substituted)phenyl-pyridin-3-yl]-N-methyl-isobutyramide as selective NK1 antagonists)

RN 474026-04-5 CAPLUS

CN Benzeneacetamide, N-[6-(1,1-dioxido-4-thiomorpholinyl)-4-(4-fluoro-2-methylphenyl)-3-pyridinyl]-N,α,α-trimethyl-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:832668 CAPLUS
DOCUMENT NUMBER: 137:337901
TITLE: Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia
INVENTOR(S): Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085458	A2	20021031	WO 2002-EP1085	20020202
WO 2002085458	A3	20031030		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2444395	AA	20021031	CA 2002-2444395	20020202
EP 1385577	A2	20040204	EP 2002-719751	20020202
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CN 1503684	A	20040609	CN 2002-808730	20020202
BR 2002009151	A	20040713	BR 2002-9151	20020202
JP 2004529931	T2	20040930	JP 2002-583031	20020202
US 2003004157	A1	20030102	US 2002-71570	20020208
ZA 2003008110	A	20050117	ZA 2003-8110	20031017
PRIORITY APPLN. INFO.:			EP 2001-109853 A	20010423
			WO 2002-EP1085 W	20020202

OTHER SOURCE(S): MARPAT 137:337901
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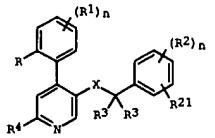

I

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H , halo , CF3, alkyl, alkoxy, cyano; R2R21 = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R3 = H, alkyl; R3R3C = cycloalkyl; R4 = H, N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl}-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (preparation given) oxone were stirred 2 days at room temperature to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate weight by 58% after 39 wk.

IT **474026-04-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia)

RN 474026-04-5 CAPLUS

CN Benzeneacetamide, N-[6-(1,1-dioxido-4-thiomorpholinyl)-4-(4-fluoro-2-methylphenyl)-3-pyridinyl]-N,α,α-trimethyl-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)